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1 RECORD OF ORAL HEARING
2
3 UNITED STATES PATENT AND TRADEMARK OFFICE
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6 BEFORE THE BOARD OF PATENT APPEALS
7 AND INTERFERENCES
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10 Ex parte JOSEPH ROBERTS and NATARAJAN SETHURAMAN
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13 Appeal 2007-3933
14 Application 09/972,245
15 Technology Center 1600
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18 Oral Hearing Held: February 12, 2008
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22 Before TONI R. SCHEINER, ERIC GRIMES, and JEFFREY N.
23 FREDMAN, *Administrative Patent Judges*.
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26 ON BEHALF OF THE APPELLANTS:
27

28 SHAUN R. SNADER, ESQUIRE
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35 The above-entitled matter came on for hearing on Tuesday, February
36 12, 2008, commencing at 9:40 a.m., at the U.S. Patent and Trademark
37 Office, 600 Dulany Street, Alexandria, Virginia, before Carol A. Lowe,
38 RPR, CCR No. 0313084, Notary Public.

1 JUDGE SCHEINER: While you're doing that, I would like you to know we
2 have an observer.

3 MR. SNADER: Sure.

4 JUDGE SCHEINER: Okay. And whenever you're ready --
5 take whatever time you need, but then once you get started you'll have 20
6 minutes.

7 MR. SNADER: Thank you. If you're ready, I'm ready to get
8 started.

9 JUDGE SCHEINER: Whenever you are.

10 MR. SNADER: Good morning. There are six grounds of
11 rejection on appeal, both anticipation and obviousness. Although the
12 references between these grounds for rejection are different, all of the
13 rejections share a common flaw. And that flaw is that the examiner has
14 misconstrued biological activity to encompass measuring immunogenicity or
15 antigenicity.

16 And, as I will explain, this is not the broadest reasonable
17 interpretation of the claims, because it runs directly contrary to the teachings
18 of the specification and the understanding of one of skill in the art.

19 To start out I want to talk just briefly about the claim subject
20 matter. Generally the claims are directed to methods of determining how a -
21 - or an active agent can be modified in order to optimize the activity of that
22 therapeutic agent.

23 More specifically, it's a method for determining the type of
24 biocompatible material, the extent of modification and the conditions for
25 modifications of a therapeutic agent with a biocompatible polymer to
26 prevent host-mediated inactivation of the therapeutic agent.

1 The background of the specification teaches that modifying a
2 therapeutic agent with a biocompatible polymer is nothing new. That's been
3 done in the past. It's known that it increases the half-life in some cases. And
4 it also can reduce the immunogenicity and antigenicity.

5 The spec background also teaches that in the past the extent or
6 the type of modification was determined by looking at a couple of things,
7 either the antigenicity and immunogenicity or an acceptable loss of
8 biological activity.

9 In other words, they modified the agent; determined the loss of
10 biological activity. And if it was within an acceptable range, that was
11 considered an acceptable modification.

12 Similar with antigenicity and immunogenicity, they looked at
13 the extent to which the modified agent would either stimulate the production
14 of antibodies or would cross-react with antibodies to the unmodified
15 therapeutic agent.

16 The background of the specification teaches that these types of
17 prior art methods of looking at immunogenicity and antigenicity were
18 flawed. They were not sufficient. Using these methods it wasn't possible to
19 predict the optimal type of modification.

20 The inventors discovered a scheme or a method to assess the
21 modification of the biological -- or the therapeutic agent that avoided the
22 problems with limiting what you're looking at to immunogenicity and
23 antigenicity.

24 JUDGE SCHEINER: Excuse me. How was loss of biological
25 activity determined? You know, where you talk about acceptable -- one of
26 the criterion -- criteria --

1 MR. SNADER: Yes.

2 JUDGE SCHEINER: -- was loss, acceptable loss of biological
3 activity, how was that --

4 MR. SNADER: Well, to a certain extent it depends on the
5 biological activity. I believe one of the prior art references -- I think it's the
6 Chinol reference -- it modified the biological agent and then used a binding
7 assay to determine how the modified compared with the unmodified.

8 And I think in that case it was avidin -- the modified agent was
9 an avidin or a variation of avidin. And the binding assay was a biotin
10 binding assay.

11 JUDGE SCHEINER: Okay.

12 MR. SNADER: Key to that is the fact that the loss of
13 acceptable binding activity was determined before the agent is administered
14 to the subject.

15 JUDGE SCHEINER: Okay.

16 MR. SNADER: Now, the claimed method which applicants
17 found to be an improvement over the prior art methods that looked at
18 immunogenicity and antigenicity administers the biological agent and then
19 after it's administered to the subject looks at the biological -- biological
20 activity of that therapeutic agent.

21 And based on looking at the biological agent after it has been
22 administered and after a booster dose has been given the applicants found
23 that this is a much better predictor of the effectiveness of the modified
24 therapeutic agent as compared to the prior art methods.

25 And specifically that's demonstrated in example three of the
26 specification where it is shown that measuring immunogenicity and

1 antigenicity was not as good of a predictor of the usefulness of the modified
2 therapeutic agent as the claimed method.

3 JUDGE SCHEINER: Okay. Well, why don't we get to what
4 the real issue here is? And that is what you mean by biological activity --

5 MR. SNADER: Yes.

6 JUDGE SCHEINER: -- based on the specification.

7 MR. SNADER: Yes.

8 JUDGE SCHEINER: And why measuring antigenicity -- apart
9 from what you say the focus of the invention is, how is measuring the
10 antigenicity or immunogenicity after a boost excluded by your specification?

11 MR. SNADER: Okay. Applicants agree -- and I don't think
12 there's any dispute -- the claims are to be given their broadest reasonable
13 interpretation during prosecution.

14 And that broadest reasonable interpretation is contained by both
15 the understanding of one of skill in the art and the teachings of the
16 specification. In other words, you can't look at the claims in context. They
17 have to be construed from the perspective of the specification.

18 Here the specification specifically addresses in the background
19 of the invention section the prior art methods of --

20 JUDGE FREDMAN: But why would we not look at page 13
21 where you define biological activity as, for example -- and they say
22 examples of biological activity -- this is at page 13 about lines nine and 10.
23 A molecule binding a receptor or antibody. It seems to me that an antigen
24 binding an antibody is the molecule binding an antibody.

25 MR. SNADER: You would look at page 13 of the
26 specification. And it is defined there, but you would not look at page 13 in

1 isolation. You would look at page 13 in the context of the entire
2 specification.

3 And in the background of the invention section it talks about
4 how measuring immunogenicity and antigenicity, something known in the
5 art -- we're doing something different. We're looking at biological activity.

6 JUDGE FREDMAN: So you think we should read a limitation
7 from the background section as against an expressed definition on page 13.

8 MR. SNADER: I don't think you have to read it against. I
9 don't think the two are inconsistent. For example, you talk about in the
10 examples here that antibody binding could be used to measure the biological
11 activity. In some cases that's correct.

12 For example, if you have a therapeutic agent that's an antibody
13 and you look at that antibody's binding to its receptor, you are looking at its
14 biological activity. That's entirely consistent with this definition as what is
15 meant by these -- this definition examples.

16 JUDGE FREDMAN: Doesn't every protein essentially have as
17 one of its biological activities the ability to bind a cognate antibody?

18 MR. SNADER: Each protein has that ability. I don't think that
19 is embraced by biological activity.

20 And the reason that's not embraced by biological activity is the
21 specification specifically states immunogenicity and antigenicity. This is
22 what these concepts are.

23 Prior art looked at these to determine the type and extent of
24 modification. We're doing something different. We're not looking at the
25 immunogenicity and antigenicity. We're looking --

26 JUDGE FREDMAN: But, in fact, you already said that if it

1 was an antibody that was -- it would be -- you could look at the antigenicity.
2 So you're saying it depends.

3 MR. SNADER: I'm -- just to be clear, you could look at,
4 depending on -- for example, if the therapeutic agent is an antibody, you --

5 JUDGE FREDMAN: Or an antigen, let's say.

6 MR. SNADER: Antigen. You could look at antibody binding
7 as a measure of the biological activity. You're not looking at
8 immunogenicity and antigenicity which are distinct concepts related to how
9 the body reacts in a narrow context to removing these as foreign matter?

10 So biological activity in some limited circumstances could be
11 looking at antibody binding, but it's the antibody binding that relates to its
12 biological function.

13 So, for example, in the Chinol reference it does -- it is a -- it is
14 directed to a pegylated avidin. I think streptavidin. They look at biotin
15 binding before it's administered to a subject to determine the acceptable loss.
16 And they do that with a biotin binding assay. They look at the biological
17 activity.

18 However, once it's administered they no longer look at the
19 biological activity. They look at the antibody binding to that pegylated
20 avidin. And that is consistent with the general prior art teachings that you
21 look at antigenicity and immunogenicity, but you don't look at the biological
22 activity.

23 Once it was administered they didn't bother to look at its ability
24 to continue binding biotin after a booster dose. They simply looked at its
25 loss of biological activity in vitro beforehand, saw that it could still bind
26 biotin, administered it and then focused on the immunogenicity and

1 antigenicity consistent with the prior art.

2 So I guess to answer your question, biological activity in some
3 limited circumstances can be binding to an antibody if that is the biological
4 effect of the therapeutic agent.

5 But in general simply looking at antibody binding is not
6 looking at biological activity. It's consistent with the prior art that was
7 distinguished which is looking at the antigenicity and immunogenicity.

8 JUDGE GRIMES: In the case of an antibody that's a
9 therapeutic agent under your definition the specific binding of that antibody
10 to its antigen would be its biological activity whereas its effect of raising
11 other antibodies to itself would be antigenicity or immunogenicity?

12 MR. SNADER: Correct. Correct. And just to be clear, there
13 are specific definitions of antigenicity and immunogenicity provided in the
14 specification; page 1, 21 to 23.

15 And that's absolutely correct; that in that case a way of looking
16 at biological activity would look at the binding to the antigen. It would not
17 involve looking at antibodies that were raised to that antibody.

18 And I'd like to talk just briefly about each of the references and
19 why they do not encompass biological activity. Generally speaking I think
20 we've already covered the fact that biological activity does not encompass
21 this concept of looking at immunogenicity and antigenicity.

22 And for that reason none of these references teach or suggest
23 the claimed method. More specifically, we've already talked a little bit
24 about the Chinol reference. It did not look at its biotin bind -- the pegylated
25 avidins, biotin binding activity after it was administered.

26 Acceptable loss was determined before it was administered.

1 And then it was simply looking at the antibodies raised to the pegylated
2 avidin.

3 Similarly, the Decker reference uses two different pegylated
4 therapeutic agents. And they were looking at the immunogenicity of these
5 pegylated agents as discussed on page 384, second column under results.

6 Now, they did look at biological binding; but, again, they did
7 that -- looked at it before being administered to determine the extent of --
8 excuse me. Determine the acceptable loss of binding activity.

9 The Alvarez reference and remaining 103 references are even
10 more distant from the claimed invention. Alvarez is just looking at a single
11 pegylated agent and determining its toxicity, specifically the incidence of
12 pancreatitis in patients treated with pegylated asparaginase as compared to
13 native asparaginase.

14 There is no measurement of biological activity after its
15 administration. There's no discussion of modifying the pegylation. It's
16 simply looking at the incidence of pancreatitis in a clinical setting.

17 Graham is very similar in its teachings in that it doesn't look at
18 the biological activity after administration. It's concerned with the toxicity
19 of these agents after administration. And toxicity of the biological -- of the
20 pegylated active agent is something known in the art and a problem that
21 people have attempted to address by modifying the types and extent of
22 modification.

23 Francis, again, looking at immunogenicity, not biological
24 activity; does not assay the biological activity after administration.

25 The remaining references are generally used to show specific
26 features of depending claims. For example, Petersen is cited to show only

1 specific polyethylene glycols.

2 That's not properly combinable with the other references for the
3 same reason -- is that all of these references even in combination lack a
4 teaching that biological activity should be assayed after administration to a
5 patient and after a booster dose is provided.

6 JUDGE SCHEINER: Do you have anything further?

7 MR. SNADER: I have nothing further. I'd be happy to --

8 JUDGE SCHEINER: Okay. I think we understand the issue.

9 MR. SNADER: Okay. Thank you very much.

10 JUDGE SCHEINER: Thank you.

11 (Whereupon, the proceedings at 9:54 a.m. were concluded.)
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